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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | 3 |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/845,514 | AOKI ET AL. | |
| | Examiner | Art Unit | |
| | Vanessa L. Ford | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9 and 17-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 17-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

1. Applicant's preliminary amendment in Paper No. 2 filed on April 30, 2001, is acknowledged. Claims 10-16 have been cancelled. Claims 1 and 17 have been amended and claim 26 has been added.

### *Declaration Defective*

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP § 602.01 and 602.02.

The oath or declaration is defective because: The full name of each inventor has not been set forth. The first name of the inventor has an initial.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

3. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Claims 1-9 are drawn to a method of treating a patient suffering from a neuromuscular disorder or condition comprising administering simultaneously to the patient a therapeutically effective amount of at least two neurotoxins selected from the groups consisting of botulinum types A, B, C, D, E, F and G.

Despite the knowledge in the art for treating neuromuscular disorders and conditions the specification fails to provide guidance regarding a method for treating such disorders and conditions claimed in this application. The specification states " that the dose of toxin depends upon the severity of the condition" (p. 9, lines 21-26). What constitutes "the severity of the condition"? How is it measured? The specification discloses that "dosages used in human therapeutic applications are roughly proportional to the mass of muscle being injected" (p. 9, lines 31-34). How can a group of patients be evaluated equally if the dosage given to each of them varies? How can the results of such a study be valid? The specification states on page 11, Example 1, "that a composition having at least 500 units of botulinum toxin type A and a lesser amount of botulinum type B is injected into the joint". What is the exact amount of botulinum toxin type A and botulinum toxin type B given to the patient? Why was a lesser amount of botulinum toxin type B given? Were there comparison studies performed to determine the effect that botulinum toxin type A, botulinum toxin type B or any of the botulinum toxins had on the patient when administered alone? What was the patient population

used in this experiment? What was the patient's medical history? Did the patient have any pre-existing medical conditions? The specification also states that" after several hours" the patient's joint was immobilized (p.11, lines 26-27). What constitutes several hours? What were the results of this experiment? The specification states "that the majority of patient's show an improvement in function both subjectively and when measured objectively" (p.11, lines 10-16). What are the specific procedures and protocols for this evaluation? How exactly are these patient's progress measured? Example 1-Example 1(f) represent the same experiment with one exception, different botulinum toxin types (i.e. botulinum toxin types B-G) are used along with botulinum toxin A. The same questions asked above can be applied to examples 1(a) – example 1(g).

The specification discloses in example 2 on page 13, a patient suffering from spasmodic torticollis. The patient is inject with "up to 300 or more units of botulinum toxins A and botulinum toxin E". What constitutes 300 units or more of the botulinum toxins used? The specification also states in this same example that "after a few hours" the patient is able to hold his head and shoulder in a "normal position". What constitutes "a few hours"? Furthermore, what constitutes a "normal position"? Patient's with pre-existing conditions may be able to hold their head's in "a normal position" that is different than what is being assumed by the applicant.

The specification discloses in example 3 – 3(e) pages 13-14, a patient suffering from essential tremor. The specification states "that the patient was treated with therapeutic amounts of botulinum A and botulinum toxin B and after two weeks the

symptoms are substantially alleviated". What constitutes a "therapeutic amount"? What constitutes "substantially alleviated"? What were the patient's symptoms? Will all patient's treated with the same therapeutic amount used in the example have their symptoms alleviated after two weeks?

The specification further discloses on pages 15-19 patients suffering from other neuromuscular disorders or conditions. The same questions that have been previously asked can be applied to these situations.

Despite the knowledge in the art for treating neuromuscular disorders using botulinum toxin type A, the specification fails to provide guidance regarding what specific protocols and procedures were used in evaluating a patient's overall state of health, a patient's severity of condition, the amount of dosage used per patient, the length of treatment and the measurement of a patient's progress are not specifically provided in the Applicant's specification. The metes and bounds of the claimed invention cannot be ascertained by the information disclosed in the specification. Therefore, one of skill in the art would require guidance, in order to make or use the claimed invention in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. The specification is being objected under 35 U.S.C. 112, second paragraph. The specification discloses example 1(a) on page 12 which appears to have the same experimental parameters of Example 1 on page 11. Are Examples 1 and 1(a) the same experiment? How are they different?

5. The specification is being objected under 35 U.S.C. 112, second paragraph. Claim 6 contains the trademark/trade name DYSPORT. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The scope of the claimed invention is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to refer to a product sold commercially by a company called Port Products Ltd located in the United Kingdom and, accordingly, the identification/description is indefinite.

6. Claims 1-9 and 17-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claims 1-9 and 17-26 recite the term "therapeutically effective amount". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "therapeutically effective amount" cannot be ascertained. Clarification as to the meaning of this term is required.

7. Claims 1-9 and 17-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claims 1-9 and 17-26 recites the term "therapeutic activity". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "therapeutic activity" cannot be ascertained. Clarification as to the meaning of this term is required.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 17-26 are rejected under 35 U.S.C. 102(b) as anticipated by Ciccarelli et al *(Applied and Environmental Microbiology, December 1977, p. 843-848).*

Claims 17-26 are drawn to a composition comprising a therapeutically effective amount of at least two neurotoxins selected for the group consisting of botulinum types A, B, C, D, E, F and G.

Ciccarelli et al teach the cultural and physiological characteristics of *Clostridium botulinum* type G and susceptibility of certain animals to its toxin (see title). Ciccarelli et al teach a composition for cross-neutralization tests comprising one volume of undiluted type G antitoxin mixed with 5 volumes of botulinal toxin types A, B, C, D, E, F and G containing 10 to 20 mouse $LD_{50}$/0.5 ml. The mixtures were incubated at 37°C for 30 minutes, after which 0.6 ml of each was injected into each member of a separate mouse pair. Toxins A through F were standard toxins in 50% glycerol, which are used to determine antitoxin levels in various sera (p. 844, 2nd column). Characteristics such as therapeutically effective amount and selected to control duration would be inherent in the composition of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's botulinum toxin composition with the botulinum toxin composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the botulinum toxin composition of the prior art does not possess the same material structural and functional characteristics of the claimed botulinum toxin composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

***Pertinent Prior Art***

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Jankovic et al, The New England Journal of Medicine, 1991, Vol 324 p. 1186-1191, Schantz et al, Microbiological Reviews, March 1992, p. 80-99 and Hatheway, Botulinum Neurotoxin and Tetanus Toxin, L.L. Simpson, Ed. published by Academic Press, Inc., 1989).*

**Status of Claims**

10. No claims are allowed.

***Conclusion***

11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
June 25, 2001

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